Robust Summaries for

Propylene Carbonate

CAS Number 108-32-7

USEPA HPV Challenge Program
Final Submission

December 17, 2004

Submitted by:

Propylene Carbonate / t-Butyl Alcohol HPV Committee

Members:

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Propylene Carbonate
High Production Volume
Robust Summaries of Existing Studies

PHYSICAL/CHEMICAL ELEMENTS

Data Point	Method	Value
1) MELTING POINT	Not Stated	-48.8 °C

Reference: Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc. 1998-1999, p. 3-145.

2) BOILING POINT	Not Stated	242 °C

Reference: Lide, D.R. (ed.). CRC Handbook of Chemistry and Physics. 79th ed. Boca Raton, FL: CRC Press Inc. 1998-1999, p. 3-145.

3) VAPOUR PRESSURE	Not Stated	0.045 mm Hg

Reference: Daubert, T.E., Danner, R.P. Physical and Thermodynamic Properties of Pure Chemicals Data Compilation. Washington, DC, Taylor and Francis, 1989.

4) PARTITION COEFFICIENT	Not Stated	Log Pow: -0.41 Temp: Not stated

Reference: Hansch, C., Leo., A., Hoekman, D., 1995. Exploring QSAR – Hydrophobic, Electronic, and Steric Constants. Washington, DC, American Chemical Society, p. 9.

5) WATER SOLUBILITY	Not Stated	175,000 mg/l @ 25 °C

Reference: Riddick, J.A., Bunger, W.B., Sakano, T.K., 1985. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY, John Wiley and Sons, p. 434.

6) PHOTODEGRADATION	Calculated	Half-life t 1/2 (preferred) : 4 days

Sensitizer (type) – hydroxyl radicals Rate Constant : 4.7x10-12 cu cm/molecule-sec @ 25 °C

Reference: Meylan, W.M., Howard, P.H., 1993. Chemosphere 26: 2293-2299.

7) STABILITY IN WATER

TEST SUBSTANCE

Identity: 100% propylene carbonate from Huntsman Chemical Company

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

Method/guideline followed (include calculated as one of the possible methods): OECD 111
Type (test type): Hydrolysis
GLP (Y/N): Yes
Year (study performed): 2004

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:

- Duration (days): pH 4@50 C = 5 days; pH 7@17 C = 59 days; pH 7@35 C = 14 days; pH 9@5 C = 7 days; pH 9@17 C = 32 hours
- Positive Controls: No
- Negative Controls: No
- Analytical procedures: GC, aliquot from initiation and termination samples tested for microbial contamination

RESULTS

Nominal
Measured value (the value with units preferably as mg/L)

Degradation % at a specified pH and temperature °C % after a specified time: Less than 10% at pH 4 and 50 C for 5 days; 49% at pH 7 and 17 C for 59 days; 66% at pH 7 and 35 C for 14 days; 65% at pH 9 and 5 C for 7 days; and 56% at pH 9 and 17 C for 32 hours.

Half-life ($t_{(1/2)}$ in days or hours at a specific pH (pH 4, 7, 9, and other) and temperature):

pH 4, 50 C – stable
pH 7, 17 C = 61.3 days
pH 7, 35 C = 8.97 days
pH 9, 5 C = 6.32 days (6.73 and 5.92 days in two replicates)
pH 9, 17 C = 1.03 days

Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results. Not determined

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use.) No measurable microbial contamination

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Author concludes that propylene carbonate is stable in water at pH 4; degradation occurs with increasing alkalinity and temperature. Rapidly degraded at pH 9 and 17 C.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1

Remarks field for Data Reliability: Guideline study, performed according to GLP and fully reported.

REFERENCES (Free Text): Leak T. 2004. Determination of Hydrolysis for Propylene Carbonate. ABC Study No. 48137. ABC Laboratories, Inc., Columbia, Missouri 65202, pp. 1-32

OTHER

Last changed (administrative field for updating): 9/13/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

8) TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS (FUGACITY)

TEST SUBSTANCE

Identity: propylene carbonate
Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.)

METHOD

Test (test type): Model estimation - EPIWIN
Method (Y/N): Y
Year (study performed): 2002

Remarks field for Test Conditions. Detail the model used (title, version and date) and the input parameters (chemical-specific, environmental conditions) as necessary.

Model = EPIWIN v. 3.10
Input parameters: water sol. = 5.957e+005
vapor pressure = 4.50E-02 mm Hg at 25 deg C
Henry LC = 3.454E-008 atm-m3/mole
Log Kow = -0.41
boiling point = 242 deg C
melting point = -48.8 deg C

RESULTS

Estimated Distribution and Media Concentration (levels II/III):
Level III Fugacity Model:

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	.946	67.8	1000
Water	46.4	360	1000
Soil	52.6	360	1000
Sediment	0.0776	1440	0

Persistence Time: 390 hr

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use including the following if available:
- Soil Adsorption coefficient: 14.85 (PCKOCWIN v. 1.66)

CONCLUSIONS: Propylene carbonate will partition mostly to water and soil.

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Conclusion of submitter.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study') = 1

Remarks field for Data Reliability: Used EPA software based on published method.

REFERENCES (Free Text): EPISuite, USEPA software v3.10, downloaded from EPA Website 2002.

OTHER

Last changed (administrative field for updating): 10/24/02 by ToxWorks

9) BIODEGRADATION

9.1 OECD 301B

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) Commercial propylene carbonate, 100% pure

METHOD

Method/guideline followed (include calculated as one of the possible methods): OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO2 evolution)"
Test Type (test type/aerobic/anaerobic): Aerobic
GLP (Y/N): Yes
Year (study performed): 2003
Contact time (units): 28 days
Innoculum: Activated sludge, domestic

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, whether there was bacterial inhibition, and detail differences from the guideline followed including the following as appropriate:

Deionized, purified, filtered water was used for this study. The microbial inoculum was activated sludge from the Columbia Wastewater Treatment Plant, Columbia, MO, which treats predominately domestic sewage. The sludge was prepared by filtering through glass wool; each reaction flask contained 1 mg/l of suspended solids. The activated sludge contained 2.6×10^6 colony forming units/ml of microorganisms, or 7.6×10^4 CFU/ml in the reaction flasks. To remove CO_2, the incoming air was passed through an Ascarite column, followed by a trap of 5N KOH.

2.4 L of the test medium was placed in each of 5 5L flasks, with 30 ml of activated sludge,

and aerated and stirred for 24 hours prior to addition of test or reference compound. Reaction flasks were chosen at random for control 1, control 2, propylene carbonate 1, propylene carbonate 2, or sodium benzoate, reference compound. Propylene carbonate was added to create a solution of 20 mg/l carbon, by addition of 127.4 mg propylene carbonate to the each of the two replicates. Sodium benzoate solution was added to the reference flask to generate a solution of 20 mg/l carbon. Additional water was added to each of the flasks to give a total volume of 3 l.

The flasks were incubated in the dark at 22 C and stirred for 29 days with continual aeration by 50-100 ml/min CO_2-free air. Off-gases were passed through 3 100 ml 0.2N KOH traps; analysis for CO_2 was performed on Days 2, 5, 7, 9, 14, 19, 23, 28, and 29. After day 28, an aliquot was removed from each reaction flask and analyzed for total carbon and inorganic carbon. Dissolved organic carbon (DOC) was calculated as the difference between total carbon and inorganic carbon.

RESULTS

Degradation % after time: 87.7% and 83.6% for replicates 1 and 2, respectively after 29 days
Results: readily biodegradable

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use, e.g. lag time, observed inhibition, excessive biodegradation, excessive standard deviation, kinetics, time required for 10% degradation and total degradation at the end of the test.)

The evolution of CO_2 was 87.7% and 83.6% for replicates 1 and 2, respectively of the theoretical CO_2 collected in the traps after 29 days.

Rate of biodegradation: Percent theoretical carbon dioxide at each analysis period

Day	% ThCO_2 Replicate 1	% ThCO_2 Replicate 2
2	7.79	7.72
5	31.4	34.7
7	56.6	57.0
9	70.2	69.3
14	80.3	78.5
19	83.7	78.6
23	86.0	82.4
28	87.7	83.5
29	87.7	83.6

In the control solution, DOC was 1.62 mg C/l at study initiation and 2.12 mg C/l at termination. These values were subtracted from the DOC values for the test flasks. For propylene carbonate, the DOC was 20.8 and 20.7 mg C/l in the two replicates at initiation, and 0.49 and 0.30 mg C/l at termination. Thus, 98% and 99% for replicates 1 and 2, respectively, of the original DOC from propylene carbonate was removed during the biodegradation study.

Biodegradation of the reference substance (sodium benzoate) reached 70.6% $ThCO_2$ by day 5 and 87.1% $ThCO_2$ by day 29, verifying that the microbial inoculum was viable and active.

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The author concludes that propylene carbonate is readily biodegradable.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, Key study

Remarks field for Data Reliability: This study was conducted in a reliable laboratory according to the current test guideline and GLPs.

REFERENCES (Free Text): Belarde D. (2003). Determination of the Ready Biodegradability of Propylene Carbonate Using the CO_2 Evolution Method. OECD 301. ABC Study No. 48069, ABC Laboratories, Inc., Columbia, Missouri 65202, pp. 1-50.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

9.1 Manostatic respirometer screening study

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) purity not stated

METHOD

Method/guideline followed: Manostatic respirometer screening study

Test Type (test type/aerobic/anaerobic): Aerobic
GLP (Y/N): No data
Year (study performed): Not stated
Contact time (units): 10 days
Innoculum: Seed from wastewater treatment plant

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, whether there was bacterial inhibition, and detail differences from the guideline followed including the following as appropriate:

- Concentration of test chemical, vehicle used, pre-acclimation conditions: not stated
- Temperature of incubation °C: Not stated
- Dosing procedure: Not stated
- Sampling frequency: Not stated
- Appropriate controls and blank system used? Not stated
- Analytical method used to measure biodegradation: Not stated
- Method of calculating measured concentrations (i.e., arithmetic mean, geometric mean, etc.): Not stated

RESULTS

Degradation % after time: 80 % during a 10-day period

- For each time period %: Not stated

Breakdown products (yes/no) If yes describe breakdown products and whether they were transient or stable in the Remarks field for Results. Not stated

Remarks field for Results (Describe additional information that may be needed to adequately assess data for reliability and use, e.g. lag time, observed inhibition, excessive biodegradation, excessive standard deviation, kinetics, time required for 10% degradation and total degradation at the end of the test.)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Submitter concludes that propylene carbonate is readily biodegradable.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 2, key study

Remarks field for Data Reliability: Not standard test; limited details available

REFERENCES (Free Text): Kayser, G et al., 1993. Git Fachz Lab 37: 416-419

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

ECOTOXICITY ELEMENTS

10) ACUTE TOXICITY TO FISH

TEST SUBSTANCE

Identity : n-Butylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): analog of Propylene carbonate

METHOD

Method/guideline followed (experimental/calculated): OECD 203
Type (test type): Semistatic, daily renewal
GLP (Y/N): Yes
Year (study performed): 1988
Species/Strain/Supplier: Rainbow trout (*Salmo gairdneri*), Parkwood Trout Farm, Kent, UK
Analytical monitoring: Yes
Exposure period (unit): 96 hours
Statistical methods: Thompson and Weil, 1952. Biometrics 8: 51-54.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations, and detail differences from the guideline followed including the following as appropriate:

- Test fish (Age/length/weight, loading, pretreatment) - Test conditions, e.g.: age- not given, length – 6.4±0.3 cm, weight - 3.96±0.8 g, acclimated to lab 17 days, acclimated to test conditions 7 days
· Details of test (static, semi-static, flow-through): Daily renewal
· Dilution water source: Laboratory tap water, dechlorinated
· Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity): hardness – 350 mg/l as $CaCO_3$, pH = 7.8 to 7.9; 9.5 to 10.1 mg O_2/l
· Stock and test solution and how they are prepared: 100, 180, 320, 560, and 1000 mg/l – direct dispersion into water
· Concentrations dosing rate, flow-through rate, in what medium
· Vehicle/solvent and concentrations
· Stability of the test chemical solutions: Verified by chemical analysis
· Exposure vessel type (e.g., size, headspace, sealed, aeration, lighting, # per treatment): Glass aquaria holding 40 l of test media

· Number of replicates, fish per replicate: 1 replicate of 10 fish per concentration
· Water chemistry in test (D.O., pH) in the control and one concentration where effects were observed: DO = 9.6 – 10.1 in control; 9.5 – 10.1 in treatment groups; pH7.8 –7.9

- Test temperature range - Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): 14.0 °C at all measurement times

RESULTS

Nominal concentrations (as mg/L): 0, 100, 180, 320, 560, 1000
Measured concentrations (as mg/L): <2.7 (loq), 103, 150, 318, 534, 875 at 0 hrs
<2.7 (loq), 99, 167, 338, 524, 907 at 24 hrs
<2.7 (loq), 97, 162, 313, 565 at 96 hrs
Unit (results expressed in what unit)
Element value (e.g. LC50, LCo, LL50, or LL0 at 48, 72 and 96 hours, etc., based on measured or nominal concentrations): LC50 at 48 = 510 (410-620), 72 = 480 (400-580), and 96 = 480 (400-580) mg/l based on nominal concentration.
Statistical results, as appropriate

Remarks field for Results. Discuss if element effect concentration is greater than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- Biological observations: Hyperactive, swimming at surface, increased pigmentation, loss of equilibrium
- Table showing cumulative mortality:

(mg/l)	hours: 6	24	48	72	96
control	0	0	0	0	0
100	0	0	0	0	0
180	0	0	0	0	0
320	0	0	0	0	0
560	1	2	7	8	8
1000	4	10	10	10	10

- Lowest test substance concentration causing 100% mortality: 1000 mg/l
- Mortality of controls: 0
- Abnormal responses
- Reference substances (if used) - results: None used
- Any observations, such as precipitation that might cause a difference between measured and nominal values.

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Submitter concludes low acute toxicity to fish from butylene carbonate and therefore also expected for propylene carbonate.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

Remarks field for Data Reliability

REFERENCES (Free Text): Douglas, M.T., Sewell, I.A., Macdonald, I.A., 1989. The Acute toxicity of n-Butylene carbonate to rainbow trout (Salmo gairdneri). Huntingdon Life Sciences Report TXO 11 (c) /89488, pp. 1-14.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

11) TOXICITY TO AQUATIC PLANTS (E.G., ALGAE)

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks. Commercial propylene carbonate, 100% pure

METHOD

Method/guideline followed (experimental/calculated): U.S. EPA OPPTS Guideline 850.5400; OECD Guideline 201
Test type: 96 hour based on growth rate
GLP (Y/N): Yes
Year (study performed): 2003
Species/Strain: unicellular green alga, *Selenastrum capricornutum*
Test details (static, semi-static, dosing rate, flow-through rate, etc.): Static
Statistical methods: All statistical analyses were performed using SAS software. The NOEC's, based on cell density, area under the growth curve, and growth rate, were estimated using a one-way analysis of variance (ANOVA) procedure and a one-tailed Dunnett's test.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test organisms: unicellular green alga, *Selenastrum capricornutum*, obtained from the Department of Botany, Culture Collection of Algae, University of Texas at Austin, on January 22, 2003. The prepared cultures were maintained in a temperature-controlled environmental chamber under continuous light. Periodically, new *Selenastrum* cultures were cloned from an existing culture derived from the parent stock. All cultures were maintained under the same conditions as those used for testing. The algal culture used for this test was three days old at test initiation.

- Test conditions
  - · Stock solutions preparation (vehicle, solvent, concentrations) and stability: propylene carbonate prepared at 1 mg/ml and confirmed by GC analysis
  - · Test temperature range: 24.2 to 25.2°C.
  - · Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): 550 ml Erlenmeyer flask, 3 replicates per dose level
  - · Dilution water source: The test medium was freshwater algal nutrient medium (FWAM) containing silicon and prepared in ABC reagent water. After preparation, the medium was pH-adjusted to 7.5 ± 0.1 using 0.1 N HCl and 0.1 N NaOH and filtered through a 0.45-µm Millipore® filter. (as described in OECD 201)
  - · Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): Below limit of quantitation for 36 organic compounds and 12 metals
  - · Lighting (quality, intensity and periodicity): Continuous lighting was provided at an average light intensity of 4,271 ± 117 lux.
  - · Temperature: 24.2-25.2 C
  - · Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: pH measured daily in all treatment groups; range 7.4 to 9.3
- Element (unit) basis (i.e. immobilization): Growth, based on Area under the curve, and growth rate
- Test design (number of replicates, individuals per replicate, concentrations): 3 replicates/concentration; 5 concentrations tested; 1 x 10^4 algae added/replicate
- Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Microscope evaluation using hemacytometer
- Exposure period: 96 hours
- Analytical monitoring: GC analysis of propylene carbonate concentration at 0, 72, and 96 hours

RESULTS

Nominal concentrations in mg/L: 0, 62.5, 125, 250, 500, 1000 mg/l
Measured concentrations in mg/L:

at initiation: <MQL , 59.2, 120, 221, 463, 929 mg/l
at 72 hours: <MQL, 49.8, 88.6, 181, 355, 773 mg/l
at 96 hours: <MQL, 27.7, 56.1, 138, 331, 740 mg/l
MQL = 12.9 mg/l

EC50, EL50, LC0, LL0, at 24, 48 hours: EC_{50}= >929 mg/l

Statistical results, as appropriate

Remarks field for Results. Discuss if element effect concentration is not less than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use including the following as appropriate:

After 96 hours of exposure, mean cell density in the control was 193×10^4 cells/mL, or 193 times the initial inoculum. The coefficient of variation was 13% for the control. The mean cell density in the propylene carbonate treatments ranged from a low of 230×10^4 cells/mL at a concentration of 120 mg total product/L to a high of 278×10^4 cells/mL at a concentration of 463 mg total product/L. Percent difference in algal growth ranged from +3.6% at a concentration of 59 and 120 mg total product/L to +7.3% at a concentration of 463 mg total product/L. Growth curves for the control and propylene carbonate treatments showed no differences. After 72 and 96 hours of exposure, there was no statistically significant reduction in cell density, area under the growth curve, or growth rate.

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The submitter concludes that propylene carbonate is not toxic to algae.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, Key study

Remarks field for Data Reliability: This study was conducted in a reliable laboratory according to the current test guideline and GLPs.

REFERENCES (Free Text): Hughes, C. (2003). Toxicity of Propylene Carbonate to the Unicellular Green Alga, *Selenastrum capricornutum*. ABC Study No. 48068, ABC Laboratories, Inc., Columbia, Missouri 65202, pp. 1-35.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks

Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

12) ACUTE TOXICITY TO AQUATIC INVERTEBRATES (E.G., DAPHNIA)

TEST SUBSTANCE

Identity: n-Butyl carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): Analog of propylene carbonate

METHOD

Method/guideline followed (experimental/calculated): OECD 202 Part 1.
Test type: Acute toxicity (immobilization)
GLP (Y/N): Yes
Year (study performed): 1988
Analytical procedures: Yes
Species/Strain: Daphnia magna (Straus)
Test details (static, semi-static, dosing rate, flow-through rate, etc.): Static
Statistical methods: No

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test organisms

· source, supplier, any pretreatment, breeding method: Laboratory culture derived from strain supplied by IRCHA in France. Reproduction by parthenogenesis
· Age at study initiation: less than 24 hours
· Control group: Yes

- Test conditions:

· Stock solutions preparation (vehicle, solvent, concentrations) and stability: Direct dispersion at 1000 mg/l
· Test temperature range: 22.0 °C
· Exposure vessel type (e.g., size, headspace, sealed, aeration, # per treatment): Glass jars containing 200 ml of test solution
· Dilution water source: Dechlorinated tap water
· Dilution water chemistry (hardness, alkalinity, pH, TOC, TSS, salinity, Ca/Mg ratio, Na/K ratio): 350 mg/l as $CaCO_3$, pH 8.
· Lighting (quality, intensity and periodicity): 16 hrs light/8 dark
· Water chemistry in test (D.O., pH) in the control and at least one concentration where effects were observed: DO = 9.4 – 9.8 mg/l, pH – 8.

- Element (unit) basis (i.e. immobilization): Immobilization
- Test design (number of replicates, individuals per replicate, concentrations): 4 replicates of 10 organisms in control and treated groups
- Method of calculating mean measured concentrations (i.e. arithmetic mean, geometric mean, etc.): Not stated
- Exposure period : 48 hours
- Analytical monitoring : Yes

RESULTS

Nominal concentrations in mg/L: 1000 mg/l
Measured concentrations in mg/L: 910 and 964 at 0 hrs; 844 and 903 at 48 hrs
Unit [results expressed in what unit]: mg/l
EC50, EL50, LC0, LL0, at 24, 48 hours: >1000 mg/l
Statistical results, as appropriate

Remarks field for Results. Discuss if element effect concentration is not less than materials solubility. Describe additional information that may be needed to adequately assess data for reliability and use including the following as appropriate:

- Biological observations
· Number immobilized as compared to the number exposed: No effects
· Concentration response with 95% confidence limits
· Cumulative immobilization: Zero
· Was control response satisfactory (yes/no/unknown)

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Submitter concludes low acute toxicity to daphnia from butylene carbonate and therefore also expected for propylene carbonate.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

Remarks field for Data Reliability

REFERENCES (Free Text): Douglas, M.T., Sewell, I.A., Macdonald, I.A., 1989. The Acute toxicity of n-Butylene carbonate to Daphnia magna. Huntingdon Life Sciences Report TXO 11 (b) /89505, pp. 1-13.

OTHER

Last changed (administrative field for updating): 3/11/02 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

HEALTH ELEMENTS

13a) ACUTE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) Purity not stated

METHOD

Method/guideline followed (experimental/calculated): equivalent to EPA 870.1100
Type (test type): Acute lethality
GLP (Y/N): Yes
Year (study performed): 1985
Species/Strain: Sprague-Dawley rats
Sex: Both
No. of animals per sex per dose: 5
Vehicle: None
Route of administration (if inhalation - aerosol, vapor, gas, particulate): Oral

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Age (Not reported) – Weight 180-219 g after fasting.
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) – 5000 mg/kg
- Doses per time period – One dose
- Volume administered or concentration: As received
- Post dose observation period: 14 days
- Exposure duration (for inhalation studies).

RESULTS

Value [LD50 or LC50] with confidence limits if calculated: >5000 mg/kg

Number of deaths at each dose level: None

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- Time of death (provide individual animal time if less than 24 hours after dosing)
- Description, severity, time of onset and duration of clinical signs at each dose level:
  No clinical signs
- Necropsy findings, included doses affected, severity and number of animals affected:
  No abnormalities in any animal
- Potential target organs (if identified in the report)
- If both sexes tested, results should be compared

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter. Submitter concludes that propylene carbonate is practically non-toxic from acute oral exposure.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1; key study

Remarks field for Data Reliability: Full study report available, adequately described, GLP study in reliable laboratory.

REFERENCES (Free Text): Mallory, V.T., Naismith, R.W., Matthews, R.J., 1985. Acute Oral Toxicity Study in Rats (14 day), Pharmakon Research International Final Report PH 402-TX-004-85, pp. 1-13.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

13b) ACUTE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) Purity not stated

METHOD

Method/guideline followed (experimental/calculated): Equivalent to EPA 870.1200
Type (test type): Acute lethality
GLP (Y/N): Yes
Year (study performed): 1986
Species/Strain: New Zealand White Rabbits
Sex: Both
No. of animals per sex per dose: 5
Vehicle: None
Route of administration (if inhalation - aerosol, vapor, gas, particulate): Dermal

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Age (Not reported) – Weight 2-3 kg.
- Doses (OECD guidelines 401 and 425 do not provide dose levels, so these must be described in detail) – 3000 mg/kg applied to abraded skin and occluded for 24 hours.
- Doses per time period – One dose
- Volume administered or concentration: As received
- Post dose observation period: 14 days
- Exposure duration (for inhalation studies).

RESULTS

Value [LD50 or LC50] with confidence limits if calculated: >3000 mg/kg
Number of deaths at each dose level: None

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available:

- Time of death (provide individual animal time if less than 24 hours after dosing)
- Description, severity, time of onset and duration of clinical signs at each dose level:
  No clinical signs
- Necropsy findings, included doses affected, severity and number of animals affected:
  No abnormalities in any animal
- Potential target organs (if identified in the report)
- If both sexes tested, results should be compared

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter. Submitter concludes that propylene carbonate is practically non-toxic following a single dermal exposure.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1

Remarks field for Data Reliability: Guideline study performed according to GLP, full report available.

REFERENCES (Free Text): Mallory, V.T., Matthews, R.J., 1986. Acute Dermal Toxicity Test in Rabbits (14 day), Pharmakon Research International Final Report PH 422-TX-006-86, pp. 1-15.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

GENETIC TOXICITY ELEMENTS

14) GENETIC TOXICITY IN VIVO (CHROMOSOMAL ABERRATIONS)

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): Purity not stated

METHOD

Method/guideline followed: Equivalent to EPA 870-5395
Type (test type): Micronucleus in mice
GLP (Y/N): Yes
Year (study performed): 1985
Species: Mouse
Strain: CRL CD-1
Sex: Both

Route of administration (if inhalation - aerosol, vapor, gas, particulate): Intraperitoneal injection
Doses/concentration levels: 1666 mg/kg
Exposure period: Single injection; subgroups were exposed for 30, 48 and 72 hours
Statistical methods: One-tailed t-test

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Age at study initiation: Seven and one-half weeks
- No. of animals per dose: 15 males and 15 females (5 for each time point): retest including 10 male and 10 female exposed for 72 hours only
- Vehicle: Distilled water
- Duration of test: 72 hours
- Frequency of treatment : Once
- Sampling times and number of samples: 30, 48, and 72 hours
- Control groups and treatment: Untreated control, positive control (TEM), one dose level of test material
- Clinical observations performed (clinical pathology, functional observations, etc.): Toxic signs
- Organs examined at necropsy (macroscopic and microscopic): Not stated
- Criteria for evaluating results (for example, cell types examined, number of cells counted in a mouse micronucleus test): 1000 PCEs
- Criteria for selection of M.T.D.: Highest non-lethal dose in preliminary test

RESULTS

Effect on mitotic index or PCE/NCE ratio by dose level by sex:

	MN/1000 PCE	PCE/NCE
H2O	0.20±0.42	1.61±0.55
TEM	54.23±16.78*	0.77±0.18*
PC-30 hr	0.50±0.97	1.76±0.42
PC-48 hr	0.30±0.48	1.43±0.50
PC-72 hr	1.20±1.40*	1.59±.037
Repeat		
H2O	0.50±0.85	1.92±0.48
TEM	48.5±9.03*	0.83±0.20*
PC-72 hr	0.30±0.57	1.77±.064

Genotoxic effects (positive, negative, unconfirmed, dose-response, equivocal): Negative

NOAEL(NOEL) (C)/LOAEL(LOEL) (C) 1666 mg/kg
Statistical results, as appropriate: * = statistically significant at p <0.05

Remarks field for Results Describe additional information that may be needed to adequately assess data for reliability and use, including the following, if available: Because positive result obtained only at 72 hours and not confirmed in repeat test with larger animal population (10/sex instead of 5/sex), the authors judged the results to be negative.

- Mortality at each dose level by sex: None
- Mutant/aberration/mPCE/polyploidy frequency, as appropriate: See table above
- Description, severity, time of onset and duration of clinical signs at each dose level and sex: Writhing after dosing; decreased body tone in some animals
- Body weight changes by dose and sex: No significant changes
- Food/water consumption changes by dose and sex: Not recorded

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The authors concluded the study was negative.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1; key study

Remarks field for Data Reliability: Guideline study performed at reliable laboratory according to GLP

REFERENCES (Free Text): Sorg, R.M., Naismith, R.W., Matthews, R.J., 1986. Micronucleus Test (MNT) – OECD, Pharmakon Research International, Inc. Final Report PH 309A-TX-004-85, pp. 1-58.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

15) GENETIC TOXICITY IN VITRO (GENE MUTATIONS)

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): Purity not stated

METHOD

Method/guideline followed: Ames method, equivalent to EPA 870-5100 except did not test *E.coli*.
Type (e.g. reverse mutation assay, gene mutation study, cytogenetic assay, mammalian cell gene mutation assay, cytogenetic assay, etc.): Reverse mutation - Ames
System of testing [bacterial, non bacterial]: Bacterial
GLP (Y/N): Yes
Year (study performed): 1985
Species/Strain or cell type and or cell line, bacterial or non-bacterial: Salmonella, TA98, TA100, TA 1535, TA1537, TA1538
Metabolic activation: S-9 from liver of Sprague-Dawley rats treated with Aroclor 1254

- Species and cell type
- Quantity
- Induced or not induced

Concentrations tested: 50, 167, 500, 1667, and 5000 ug/plate as preincubation assay
Statistical Methods: Moore and Felton, 1983. Mutat. Res. 119: 95-102.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations. Detail differences from the guideline followed including the following as appropriate:

- Test Design

· Number of replicates: Three
· Frequency of Dosing: Pre-incubation assay
· Positive and negative control groups and treatment
· Number of metaphases analyzed
- Solvent
- Description of follow up repeat study
- Criteria for evaluating results (e.g. cell evaluated per dose group): triple untreated control rate or statistically significant trend

RESULTS

Result:
Cytotoxic concentration
- With metabolic activation: >5000 µg/plate
- Without metabolic activation: >5000 µg/plate

Genotoxic effects (e.g. positive, negative, unconfirmed, dose-response, equivocal)

- With metabolic activation: Negative
- Without metabolic activation: Negative

Statistical results, as appropriate

Remarks field for Results. Note test-specific confounding factors such as pH, osmolarity, whether substance is volatile, water soluble, precipitated, etc., particularly if they effect the selection of test concentrations or interpretation of the results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.

- Frequency of reversions/mutations/aberrations, polyploidy as appropriate
- Precipitation concentration if applicable
- Mitotic index

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The authors concluded that the test material was negative in the Ames assay.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

Remarks field for Data Reliability: Guideline study performed according to GLP and reliable laboratory

REFERENCES (Free Text): Godek, E.G., Naismith, R.W., Matthews, R. J., 1985. Ames Salmonella/Microsome Liquid Pre-Incubation Assay. Pharmakon Research International Inc Final Report PH 301-TX-006-85, pp. 1-22.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

16a) REPEATED DOSE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): Purity not stated

METHOD

Method/guideline followed: Equivalent to OECD 408
Test type: 90 day Oral Study
GLP (Y/N): Yes
Year (study performed): 1988
Species: Rat
Strain: Charles River Sprague-Dawley derived
Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Gavage
Duration of test : 90 Days
Doses/concentration levels: 0, 1000, 3000, 5000 mg/kg/day
Sex: Both
Exposure period: 90 days
Frequency of treatment: Five days/week for 13 weeks
Control group and treatment : Distilled water by gavage
Post exposure observation period: Additional groups of control and high-dose observed for 28 days post dosing.
Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

· Age at study initiation: 40 days
· No. of animals per sex per dose - Study Design: 10, additional 5/sex/dose terminated after 30 days; additional 10/sex for control and high dose held 28 days post dosing.

· Vehicle: None, dosed as received.
· Satellite groups and reasons they were added: Control and high-dose for recovery.
· Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, hematology (RBC, Hemat., PCV, WBC, diff., plt) and clinical chemistry (glu, crea, tbil, bun, ALT, AST, GGT, Tpro, alb, glob, Na, K, Cl, Ca, P) at 30 and 90 days. Ophthalmoscopy pretest at 30 and 90 days.
· Organs examined at necropsy (macroscopic and microscopic): brain, pituitary, thyroid, parathyroid, thymus, lungs, trachea, heart, sternum with bone marrow, salivary glands, liver, spleen, kidneys, adrenals, pancreas, gonads, uterus, accessory sex organs, aorta, skin, esophagus, nasal turbinates, stomach, duodenum, jejunum, ileum, cecum, colon, rectum,

urinary bladder, lymph node, mammary gland, skeletal muscle, peripheral nerve, three levels of spinal cord, lachrymal glands.

RESULTS

NOAEL (NOEL): 5000 mg/kg/day
LOAEL (LOEL)
Actual dose received by dose level by sex, if known,
Toxic response/effects by dose level: No adverse effects seen
Statistical results, as appropriate:

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.

- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Description, severity, time of onset and duration of clinical signs: No treatment effect
- Ophthalmologic findings incidence and severity: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: Few clinical chemistry significant differences, not consistent between sexes or 30 vs. 90 days
- Mortality and time to death: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: Few organ weight differences, not consistent between sexes or 30 vs 90 days
- Histopathology incidence and severity: No treatment effect

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Authors concluded there were no treatment-related effects.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

Remarks field for Data Reliability: Guideline study conducted according to GLP in reliable laboratory

REFERENCES (Free Text): Margitich, D.J., 1989. Subchronic Oral toxicity in Rats. Pharmakon Research International, Inc. Final Report Ph 470-TX-001-88, pp. 1 – 158, plus two appendices.

OTHER

Last changed (administrative field for updating): 1/27/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks [Note - Use for any other comments necessary for clarification.]

16b) REPEATED DOSE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): Purity not stated

METHOD

Method/guideline followed: Equivalent to OECD 408
Test type: 14 Week Aerosol Inhalation Study
GLP (Y/N): Yes
Year (study performed): 1991
Species: Rat
Strain: Harlan F344
Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Aerosol inhalation
Duration of test : 93 Days
Doses/concentration levels: 0, 100, 500, 1000 mg/m^3;
diameter (MMAD) = 4.9 microns +/- 2.5 gsd
Sex: Both
Exposure period: 93 days
Frequency of treatment: Six hours/day five days/week for 13 weeks
Control group and treatment : Clean air
Post exposure observation period: No
Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

· Age at study initiation: 47 days
· No. of animals per sex per dose - Study Design: 10, additional 5/sex/dose for neurotoxicity evaluation; additional 2/sex for control and high dose for neurotoxicity evaluation after a single exposure.

· Vehicle: None
· Satellite groups and reasons they were added: Control and high dose for neurotoxicity evaluation after a single exposure.
· Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, hematology (RBC, Hemat., PCV, WBC, diff., plt) and clinical chemistry (glu, crea, tbil, cbil, ubil, bun, ALT, AST, GGT, SDH, ALK, Tpro, alb, glob, Na, K, Cl, Ca, P) at 90 days. Ophthalmoscopy pretest and 90 days, food and water consumption first 4 weeks, body weights weekly. FOB and motor activity after six and thirteen weeks. FOB one and 23 hours after single 6-hour exposure. For FOB, animals were placed in clean clear cage for 2 minutes while observed for horizontal and vertical movement, convulsions, tremors, stereotypy, piloerection, respiration, urination, gait, and acoustic startle response. The animal was removed and observed for pupil size and response to light, vocalization, salivation, mouthbreathing, lacrimation, diarrhea, visual placing and muscle tone. Catatonia, forelimb and hindlimb grip strength, surface and air righting reflexes performance on a rotating treadmill, positive geotropism, toe and tail withdrawal reflexes, hind leg splay, and rectal temperature were recorded using simple equipment. Motor activity was determined using San Diego Instruments test equipment.
· Organs examined at necropsy (macroscopic and microscopic): brain, pituitary, thyroid, parathyroid, thymus, lungs, trachea, esophagus, nasopharyngeal tissues, larynx, heart, sternum with bone marrow, salivary glands, liver, spleen, kidneys, adrenals, pancreas, gonads, uterus, accessory sex organs, aorta, skin, nasal turbinates, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, urinary bladder, lymph node, mammary gland, skeletal muscle, peripheral nerve, three levels of spinal cord, lachrymal glands, Zymbal's glands.

RESULTS

NOAEL (NOEL): 100 mg/m^3
LOAEL (LOEL): 500 mg/m^3
Actual dose received by dose level by sex, if known,
Toxic response/effects by dose level: Inflammation of ocular tissues in 2 males at 500 and 4 males at 1000 mg/m^3.
Statistical results, as appropriate:

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide at a minimum qualitative descriptions of elements where dose effect related observations were seen.

- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Description, severity, time of onset and duration of clinical signs: Periocular swelling at 500 and 1000 mg/m^3

- Ophthalmologic findings incidence and severity: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: No treatment effect
- Mortality and time to death: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: Few organ weight differences, not consistent between sexes or supported by histopathologic findings.
- Histopathology incidence and severity: No treatment effect

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Authors concluded there was mild eye irritation at 500 and 1000 mg/m^3.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

Remarks field for Data Reliability: Guideline study performed according to GLP at reliable laboratory

REFERENCES (Free Text): Burleigh-Flayer, H.D., Nachreiner, D.J., Kintigh, W.J., 1991. Propylene carbonate: Fourteen-Week aerosol inhalation study on rats with neurotoxicity evaluation. Bushy Run Research Center Final Report 52-637, pp. 1 – 56, plus 12 appendices.

OTHER

Last changed (administrative field for updating): 2/06/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks [Note - Use for any other comments necessary for clarification.]

16c) REPEATED DOSE TOXICITY

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.): purity not stated

METHOD

Method/guideline followed:
Test type: Dermal Carcinogenicity Study

GLP (Y/N): Yes
Year (study performed): 1987-1991
Species: Mouse
Strain: Jackson C3H/HeJ
Route of administration, oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: dermal
Duration of test : 104 weeks
Doses/concentration levels: 0, 50 µl/mouse twice/week (~1500-2000 mg/kg/dose)
Sex: Male
Exposure period: 104 weeks
Frequency of treatment: Twice/week for 104 weeks
Control group and treatment : No treatment
Post exposure observation period: No
Statistical methods: One-way analysis of variance.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Test Subjects

· Age at study initiation: 8 weeks
· No. of animals per sex per dose: 50 males only

· Vehicle: None
· Satellite groups and reasons they were added: None
· Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, body weights weekly.
· Organs examined at necropsy (macroscopic and microscopic): Necropsy: Carcass and muscular/skeletal systems, external surfaces and orifices, cranial cavity and brain, neck and associated organs, thoracic, abdominal and pelvic cavities and organs. Microscopic Examination: Skin, nodules, masses and lesions.

RESULTS

NOAEL (NOEL): 1500-2000 mg/kg (twice/week)
LOAEL (LOEL)
Actual dose received by dose level by sex, if known,
Toxic response/effects by dose level: None reported
Statistical results, as appropriate:

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following if available. Provide

at a minimum qualitative descriptions of elements where dose effect related observations were seen.

- Body weight: No treatment effect
- Food/water consumption: Not measured
- Description, severity, time of onset and duration of clinical signs: No treatment effect
- Ophthalmologic findings incidence and severity: Not measured
- Hematological findings incidence and severity: Not measured
- Clinical biochemistry findings incidence and severity: Not measured
- Mortality and time to death: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: Not measured
- Histopathology incidence and severity: No treatment effect

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: Authors concluded there was no increase in tumors.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, Key study

Remarks field for Data Reliability: GLP study conducted at reliable laboratory; full report available.

REFERENCES (Free Text): Garman, R.H., Van Miller, J.P., Negley, J.E., 1991. Chronic Dermal Carcinogenicity Studies in C3H/HeJ Male Mice. Bushy Run Research Center Final Report 52-527, pp. 1 – 143, plus 8 appendices.

OTHER

Last changed (administrative field for updating): 1/28/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks [Note - Use for any other comments necessary for clarification.]

17) TOXICITY TO REPRODUCTION

TEST SUBSTANCE

Identity: Propylene Carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) Purity not stated

METHOD

Method/guideline followed: Assessment of reproductive organs in a 90 day study
Type (one generation, two generation, etc.): 90 Day Oral, Evaluation of Sex organs
GLP (Y/N): Yes
Year (study performed): 1988
Species: Rat
Strain: Charles River Sprague-Dawley derived
Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Gavage
Doses/concentration levels: 0, 1000, 3000, 5000 mg/kg/day
Sex: Both
Control group and treatment: Yes
Frequency of treatment: Five days/week
Duration of test: 13 weeks
Premating exposure period for males (P and F1) as appropriate
Premating exposure period for females (P and F1) as appropriate
Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests.

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
- Test animals
· Number, age, sex per dose for P, F1 and F2, if appropriate: 10/sex/group at 40 days old
- Test design
· Vehicle: None
· Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate: Five days/week
- Parameters assessed during study P and F1 as appropriate
· Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily observations, hematology. Clinical chemistry at 30 and 90 days
· Estrous cycle length and pattern (number of days spent in each phase): Not assessed
· Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not assessed
- Parameters assessed during study F1 and F2, as appropriate
· Clinical observations performed and frequency (weight gain, growth rate, etc.): Weekly BW
· Others, for example anogenital distance, if performed
· Organs examined at necropsy (macroscopic and microscopic): Ovaries, uterus, testes, accessory sex organs

RESULTS

NOAEL (NOEL) and LOAEL (LOEL) for P, F1 and F2, as appropriate: 5000 mg/kg/day

Actual dose received by dose level by sex if known

Statistical results, as appropriate

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available: Assessment of reproductive organs from 90 day study

- Parental data and F1 as appropriate, provide at a minimum qualitative descriptions of elements were dose related observations were seen
- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Description, severity, time of onset and duration of clinical signs: No treatment effect
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: No treatment effect
- Mortality: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: No treatment effect
· Histopathology incidence and severity: No effect on ovaries, testes or accessory sex organs

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The submitter concludes that propylene carbonate had no effect on reproductive organs

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 2, key study

Remarks field for Data Reliability: Not a guideline study of reproductive effects, but indicates no effects would be expected.

REFERENCES (Free Text): Margitich, D.J., 1989. Subchronic Oral toxicity in Rats. Pharmakon Research International, Inc. Final Report Ph 470-TX-001-88, pp. 1 – 158, plus two appendices.

OTHER

Last changed (administrative field for updating): 2/06/04 by ToxWorks

Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)

TEST SUBSTANCE

Identity: Propylene Carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) Purity not stated

METHOD

Method/guideline followed: Assessment of reproductive organs in a 14 week study
Type (one generation, two generation, etc.): Assessment of reproductive organs in a 14 week study
GLP (Y/N): Yes
Year (study performed): 1991
Species: Rat
Strain: Harlan F344
Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Aerosol inhalation
Doses/concentration levels: 0, 100, 500, 1000 mg/m^3, diameter MMAD) = 4.9 +/- 2.5 gsd
Sex: Both
Control group and treatment: Clean air
Frequency of treatment: 93 Days
Statistical methods: One-way analysis of variance, followed by Dunnett's or Tukey's tests

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:
- Test animals:
· Number, age, sex per dose for P, F1 and F2, if appropriate: 10 per sex per group, 47 days old
- Test design
· Vehicle: None
· Dosing schedules and pre and post dosing observations periods for P, F1 and F2, if appropriate
- Parameters assessed during study P and F1 as appropriate
· Clinical observations performed and frequency (clinical pathology, functional observations, etc.): Daily
· Estrous cycle length and pattern (number of days spent in each phase): Not assessed
· Sperm examination (epididymal or vas sperm, concentration, motility, morphology): Not assessed
- Parameters assessed during study F1 and F2, as appropriate
· Clinical observations performed and frequency (weight gain, growth rate, etc.): Weekly BW
· Organs examined at necropsy (macroscopic and microscopic): Ovaries, uterus, testes, accessory sex organs

RESULTS

NOAEL (NOEL) and LOAEL (LOEL) for P, F1 and F2, as appropriate: 1000 mg/m^3 for reproductive organs

Actual dose received by dose level by sex if known

Parental data and F1 as appropriate (toxic response/effects with NOAEL value). Provide at a minimum qualitative descriptions of elements were dose related observations were seen: No effect on reproductive organs. Periocular swelling seen in a few males at 500 and 1000 mg/m^3

Statistical results, as appropriate

Remarks field for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available:

- Parental data and F1 as appropriate, provide at a minimum qualitative descriptions of elements were dose related observations were seen
- Body weight: No treatment effect
- Food/water consumption: No treatment effect
- Description, severity, time of onset and duration of clinical signs
- Hematological findings incidence and severity: No treatment effect
- Clinical biochemistry findings incidence and severity: No treatment effect
- Mortality: No treatment effect
- Gross pathology incidence and severity: No treatment effect
- Organ weight changes: No treatment effect
· Histopathology incidence and severity: No effect on ovaries, testes or accessory sex organs

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter: The submitter concludes that propylene carbonate had no effect on reproductive organs

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 2, key study

Remarks field for Data Reliability: Not a guideline study of reproductive effects, but indicates no effects would be expected.

REFERENCES (Free Text): Burleigh-Flayer, H.D., Nachreiner, D.J., Kintigh, W.J., 1991. Propylene carbonate: Fourteen-Week aerosol inhalation study on rats with neurotoxicity evaluation. Bushy Run Research Center Final Report 52-637, pp. 1 – 56, plus 12 appendices.

OTHER

Last changed (administrative field for updating): 02/06/04 by ToxWorks
Order number for sorting (administrative field)

18) DEVELOPMENTAL TOXICITY/TERATOGENICITY

TEST SUBSTANCE

Identity: Propylene carbonate

Remarks field for Test Substance (Use for any pertinent, test substance-specific remarks.) Purity not stated

METHOD

Method/guideline followed
GLP (Y/N): Yes
Year (study performed): 1988
Species: Rat
Strain: Charles River Sprague-Dawley
Route of administration - oral (gavage, drinking water, feed), dermal, inhalation (aerosol, vapor, gas, particulate), other: Oral (gavage)
Doses/concentration levels: 0, 1000, 3000 and 5000 mg/kg/day
Sex: Females
Exposure period: Days 6-15 of gestation
Frequency of treatment: Once per day
Control group and treatment: Distilled water by gavage
Duration of test: Days 6-20 of gestation
Statistical methods: Anova, followed by Dunnett's

Remarks field for Test Conditions. Detail and discuss any significant protocol deviations and detail differences from the guideline followed including the following as appropriate:

- Age at study initiation: 80-120 days
- Number of animals per dose per sex: 27
- Vehicle: None
- Clinical observations performed and frequency : Daily
- Mating procedures (M/F ratios per cage, length of cohabitation, proof of pregnancy): One male with one or two females until signs of copulation
- Parameters assessed during study (maternal and fetal): Daily toxicologic signs; body weight days 6, 9, 12, 15, 20; and food consumption days 0-6, 6-13, 13-20.

- Organs examined at necropsy (macroscopic and microscopic): Complete necropsy; number and location of viable fetuses, early and late resorptions, total implantations and corpora lutea, half of fetuses soft tissue analysis, other half skeletal analysis.

RESULTS

NOAEL (NOEL) and LOAEL (LOEL) maternal toxicity: 1000 mg/kg/day
NOAEL (NOEL) and LOAEL (LOEL) developmental toxicity: 5000 mg/kg/day
Actual dose received by dose level by sex if available
Maternal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen. Mortality, salivation, decreased activity, abnormal gait, dyspnea, cyanosis
Fetal data with dose level (with NOAEL value). Provide at a minimum qualitative descriptions of responses where dose related effects were seen. No effects
Statistical results, as appropriate

Remarks for Results. Describe additional information that may be needed to adequately assess data for reliability and use include the following when there are dose related effects if available: Maternal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen.

- Mortality and day of death: at 3000 mg//kg/day: days 9 and 13;
  at 5000 mg/kg/day: days 10, 10, 11, 11, 14
- Number pregnant per dose level: At cesarean section, 27, 26, 23, 22 pregnant at 0, 1000, 3000 and 5000 mg/kg/day
- Number aborting: None
- Number of resorptions, early/late if available:

- Number of implantations:		15.4	15.2	15.6	14.9
- Pre and post implantation loss, if available:	pre (%):	8.0	6.3	10.2	10.6
	post (%)	4.7	9.7	5.2	11.7
- Number of corpora lutea (recommended):		17.0	16.3	17.5	16.6

- Duration of Pregnancy: Terminated day 20 of gestation
- Body weight: Decreased body weight gain at 5000 mg/kg/day: 53 g vs 77 g in control days 6-15
- Food/water consumption: Reduced food consumption at 3000 and 5000 mg/kg/day days 6-13
- Description, severity, time of onset and duration of clinical signs: Salivation, in some rats days 6-15, decreased activity in some rats days 6-15 at 3000 and 5000 mg/k/day
- Hematological findings incidence and severity: Not examined
- Clinical biochemistry findings incidence and severity: Not examined
- Gross pathology incidence and severity: No adverse effects
- Organ weight changes, particularly effects on total uterine weight: Not examined
- Histopathology incidence and severity: Not examined
- Fetal data, provide at a minimum qualitative descriptions of responses where dose related effects were seen

· Litter size and weights:	size	14.6	13.6	14.7	13.2

	weight	3.8	3.9	3.8	3.6

· Number viable (number alive and number dead)

· Sex ratio:	% male	53	48	51	50

· Postnatal growth (depending on protocol)
· Postnatal survival (depending on protocol)
· Grossly visible abnormalities, external, soft tissue and skeletal abnormalities: No significant differences

CONCLUSIONS

Remarks field with the ability to identify source of comment, i.e. author and/or submitter. Submitter concludes that propylene carbonate does not induce developmental effects.

DATA QUALITY

Reliabilities (Klimisch Code, if used, possibly a flag if 'key study'): 1, key study

Remarks field for Data Reliability

REFERENCES (Free Text): Margitich, D.J. (1988). Developmental toxicity study in rats. Pharmakon Research International, Inc. Final Report PH 328-TX-001-88, pp. 1-44, plus 2 appendices.

OTHER

Last changed (administrative field for updating): 02/06/04 by ToxWorks
Order number for sorting (administrative field)

Remarks field for General Remarks (Use for any other comments necessary for clarification.)